201-14938B

Fyrol 6
HPV Robust Summaries
Akzo Nobel Functional Chemicals LLC
December 2003

1. Substance Information

CAS Number:	2781-11-5
Chemical Name:	Phosphonic acid, [[bis (2-hydroxyethyl) amino] methyl]-diethyl ester
Structural Formula:	$C_9H_{22}NO_5P$
Other Names:	Diethyl [(diethanolamino) methyl] phosphonate; Fyrol 6
Exposure Limits:	None

2. Physical – Chemical Properties

2.1. Melting Point:

Identity:	Fyrol 6; CAS# 2781-11-5
Method:	EPIWIN Computer Model
GLP:	Not applicable
Year:	Not applicable
Value:	83.21°C
Decomposition:	Not available
Conclusions:	The melting point of Fyrol 6 is estimated to be 83.21°C.
Reliability:	4
Reference:	1
Remarks:	Fyrol 6 is a liquid but this estimation indicates that it will be a solid. A melting point study should be conducted.
Additional References for Melting Point Studies:	None

2.2. Boiling Point:

Identity:	Fyrol 6; CAS# 2781-11-5
Method:	EPIWIN Computer Model
GLP:	Not applicable
Year:	Not applicable
Value:	379.4°C
Decomposition:	Not available

Conclusions:	The boiling point of Fyrol 6 is estimated to be 379.37°C.
Reliability:	1
Reference:	2
Remarks:	None
Additional References for Melting Point Studies:	None

2.3. Vapor Pressure:

Identity:	Fyrol 6; CAS# 2781-11-5; Lot 0106B-12; purity – 70-90%
Method:	OECD 104
GLP:	No
Year:	2000
Value:	0.43 mm Hg
Temperature° C:	20
Pressure Unit:	MmHg
Decomposition:	Not reported
Conclusions:	The vapor pressure of Fyrol 6 is C is 0.43 mmHg.
Reliability:	2
Reference:	3
Remarks:	Isoteniscope method
Additional Reference for Vapor Pressure Studies:	None

2.4. Partition Coefficient (log Kow):

Identity:	Fyrol 6; CAS# 2781-11-5; Lot 0106B-12; purity – 70-90%
Method:	OECD 107
GLP:	No
Year:	2001
Log Kow:	-0.72
Temperature°C:	25
Conclusions:	The log Kow of Fyrol 6 is -0.72
Reliability:	2
Reference:	4

Remarks:	None
Additional References for Partition Coefficient Studies:	None

2.5. Water Solubility:

Identity:	Fyrol 6; CAS# 2781-11-5; Lot 0106B-12; purity – 70-90%
Method:	OECD 105
GLP:	No
Year:	2001
Value at temperature°C:	900 g/L at 25°C
Description of solubility:	Clear
PH value and concentration at temperature °C:	Not reported
Pka value at 25°C:	Not reported
Conclusions:	The water solubility of Fyrol 6 is 900 g/L.
Reliability:	2
Reference:	5
Remarks:	Flask method
Additional References for Water Solubility Studies:	None

3. Environmental Fate

3.1. Photodegradation:

Identity:	Fyrol 6; CAS# 2781-11-5
Method:	EPIWIN Computer Model
GLP:	Not applicable
Type:	Not applicable
Year:	Not applicable
Light Source:	Not applicable
Light Spectrum (nm):	Not applicable
Half-life:	0.898 hours
Breakdown Products:	Not available
Conclusions:	The half-life in the atmosphere for Fyrol 6 is estimated to be 0.898 hours.
Reliability:	1
Reference:	6
Remarks:	None
Additional References for Photodegradation Studies:	None

3.2. Transport (Fugacity):

Identity:	Fyrol 6; CAS# 2781-11-5			
Method:	EPIWIN Computer Model			
GLP:	Not applicable			
Type:	Not applicable			
Year:	Not applicable			
Media:	Air, Water, Soil, Sediment			
Distributions:	Compartment	Released 100% to air	Release 100% to water	Release 100% to soil
	Air	6.8	3.98×10^{-4}	0.0213
	Water	35	99.8	31.8
	Soil	58.2	3.4×10^{-3}	68.1
	Sediment	0.0645	0.184	0.0681
Conclusions:	Fyrol 6 is distributed primarily to water and soil.			
Reliability:	1			
Reference:	7			
Remarks:	When released equally to air, water and soil, Fyrol 6 is distributed 0.2% to air, 58.3% to water, 41.4% to soil and 0.1% to sediment.			
Additional References for Transport (Fugacity) Studies:	None			

3.3. Biodegradation:

Identity:	Fyrol 6; CAS# 2781-11-5; Batch 8106 J-5-2; purity not given
Method:	OECD 301D
Type:	Modified Sturm Test
GLP:	Yes
Year:	1990
Degradation% after time:	15% (10 mg/L) and 19% (20 mg/L) at 28 days
Breakdown Products:	Not determined
Concentration Of Test Chemical:	10 mg/L, 20 mg/L
pH Of Test Media:	6.87-7.29
Conclusions:	Fyrol 6 is not readily biodegradable.
Reliability:	1
Reference:	8
Remarks:	Source of test organism was activated sludge obtained from a municipal sewage treatment plant
Additional References for Biodegradation Studies:	None

4. Ecotoxicity

4.1. Acute Toxicity to Fish:

Identity:	Fyrol 6; CAS# 2781-11-5; Batch 8106 J-5-2; purity not given
Method:	OECD 203
Type:	Static
GLP:	Yes
Year:	1990
Species/Strain:	Rainbow trout, *salmo gairdneri*
Supplier:	Hauxton Fishery Services, Cambridge, England
Analytical Monitoring:	None
Exposure Period:	96 hours
Nominal Concentrations:	1000, 1800, 3200, 5600 and 10000 mg/L
LC50:	>10000 mg/L
Conclusions:	The LC50 of Fyrol 6 is >10000 mg/L.
Reliability:	1
Reference:	9
Remarks:	There was 20% mortality at 3200 mg/L but none at higher

	concentrations. Ten fish were used in each test group. The water hardness was 216-242 mg/CaCO3/L. The pH was 7.08-8.32. The temperature was 14.1-15.0°C.
Additional References for Acute Toxicity to Fish Studies:	None

5. Mammalian Toxicity

5.1. Acute Toxicity:

5.1.1. Oral

Identity:	Fyrol 6; CAS# 2781-11-5; Lot# 2781115; purity not given
Method:	EPA Guidelines for pesticide registration; Fed. Reg. 43:163, 37336-37402 (1978); OECD (1981)
Type:	Acute Oral LD50
GLP:	Yes
Year:	1983
Species/Strain:	Rat/Sprague-Dawley
Sex:	M/F
No. Of Animals Per Sex Per Dose:	10
Vehicle:	Corn oil
Route Of Administration:	Oral gavage
Time Of Observation Period:	14 Days
Doses Administered:	5000 mg/kg
LD50:	>5000 mg/kg
Conclusions:	The oral LD50 of Fyrol 6 in rats is greater than 5000 mg/kg.
Reliability:	1
Reference:	10
Remarks:	Clinical signs of toxicity were mild depression, piloerection, alopecia and red facial stains. All animals appeared normal by day 2. The only effect seen at necropsy was reddened intestines.
Additional References for Acute Oral Toxicity Studies:	None

5.1.2. Dermal

Identity:	Fyrol 6; CAS# 2781-11-5; Lot# 2781115; purity not given

Method:	EPA Guidelines for pesticide registration; Fed. Reg. 43:163, 37336-37402 (1978); OECD (1981)
Type:	Acute Dermal
GLP:	Yes
Year:	1983
Species/Strain:	Rabbit/Stauffland albino
Sex:	M/F
No. Of Animals Per Sex Per Dose:	5
Vehicle:	None
Route Of Administration:	Dermal
Time Of Observation Period:	14 Days
Doses Administered:	2000 mg/kg for 24 hours
LD50:	>2000 mg/kg
Conclusions:	The dermal LD50 of Fyrol 6 in rabbits is greater than 2000 mg/kg.
Reliability:	1
Reference:	11
Remarks:	There was no mortality. Clinical signs of toxicity were mild depression. All animals appeared normal by day 1. Local dermal effects included mild erythema and edema. There were no adverse effects at necropsy.
Additional References for Acute Dermal Toxicity Studies:	None

5.1.3. Skin Irritation

Identity:	Fyrol 6; CAS# 2781-11-5; Lot# 2781115; purity not given
Method:	DOT Fed. Reg. Title 49, Part 173 Appendix II 10/1/77
Type:	Skin irritation
GLP:	Yes
Year:	1983
Species/Strain:	Rabbit/Stauffland albino
Sex:	M/F
No. Of Animals:	6
Vehicle:	None
Route Of Administration:	Dermal
Time Of Exposure:	4 hours
Time Of	4 and 48 hours

Observation Period:	
Concentration Of Test Material:	0.5mL
Results:	There was no erythema or edema at any observation period. Draize scoring used.
Conclusions:	Fyrol 6 was not irritating to rabbits following dermal exposure for 4 hours.
Reliability:	1
Reference:	12
Remarks:	None
Additional References for Acute Dermal Irritation Studies:	None

5.1.4. Eye Irritation

Identity:	Fyrol 6; CAS# 2781-11-5; Lot# 2781115; purity not given
Method:	EPA Guidelines for pesticide registration; Fed. Reg. 43:163, 37336-37402 (1978); OECD (1981)
Type:	Eye irritation
GLP:	Yes
Year:	1983
Species/Strain:	Rabbit/Stauffland albino
Sex:	M/F
No. Of Animals:	9
Vehicle:	None
Route Of Administration:	Ocular
Time Of Exposure:	Eyes of 3 animals washed after 20-30 seconds of exposure. Eyes of the other 6 animals were not washed.
Time Of Observation Period:	24, 48, 72 hours and 4, 7 days
Concentration Of Test Material:	0.1mL
Results:	There was mild conjunctival irritation in 6 rabbits with unwashed eyes and no effects in the 3 rabbits with washed eyes. The irritation cleared by the 72 hour observation period. Draize scoring used.
Conclusions:	Fyrol 6 was mildly irritating to rabbits.
Reliability:	1
Reference:	13
Remarks:	None

Additional References for Acute Dermal Irritation Studies:	None

5.2. Repeated Dose Toxicity:

Identity:	Fyrol 6; CAS# 2781-11-5; Lot# 1106 L-1; purity – 90.7%
Method:	Repeat Dose - Oral
Type:	13-Week Oral Toxicity
GLP:	Yes
Year:	1983
Species/Strain:	Rat/Sprague-Dawley
Sex:	M/F
No. Of Animals Per Sex Per Dose:	22
Vehicle:	Corn oil
Route of Administration:	Oral gavage
Time of Observation Period:	13 weeks
Doses Administered:	20, 100, 500 mg/kg/day
Frequency of Treatment:	Once daily for 13 weeks, 7 days per week
NOAEL:	500 mg/kg/day
LOAEL:	>500 mg/kg/day
Toxic Response By Dose Level:	Control: Mortality - three females (dosing accident) and three males (dosing accident); Macroscopic exam - enlarged liver in eight animals. 500 mg/kg/day: Mortality – one male (dosing accident) and six females (dosing accident); Clinical signs – alopecia, darker coloration of eyes, chromorhinorrhea; Clinical chemistry – increase in white blood cells; lower hemoglobin and hematocrit; Macroscopic exam – discoloration of lungs, thymus, liver and kidney and enlarged liver; Organ weights – significant increase in mean absolute and relative liver weight and an increase in mean absolute and relative kidney weight; Microscopic exam – very slight hepatocellular hypertrophy, cytoplasmic eosinophilia of centrilobular hepatocytes. 100 mg/kg/day – Mortality – five males (dosing accident) and two females (dosing accident); Clinical signs – alopecia; Clinical

	chemistry – decrease in red blood cells; Macroscopic exam – discoloration of lungs, liver and kidney and enlarged liver; Organ weights – increase in mean relative liver and absolute and relative kidney weight; Microscopic exam – very slight hepatocellular hypertrophy, cytoplasmic eosinophilia of centrilobular hepatocytes. 20 mg/kg/day – Mortality – One male (dosing accident) and three females (dosing accident); Clinical signs – alopecia; Clinical chemistry – decrease in red blood cells; Macroscopic exam – discoloration of lungs and kidney and enlarged liver; Organ weights – no changes; Microscopic exam – no changes. There were no signs of functional changes in the kidney and liver of animals in any dose groups.
Conclusions:	Fyrol 6 administered daily by oral gavage to rats for 13 weeks resulted in minor histopathological changes in the liver at doses of 100 and 500 mg/kg/day. These results were considered an adaptive rather than a toxic response to Fyrol 6. The NOAEL was 500 mg/kg/day.
Reliability:	1
Reference:	14
Remarks:	None
Additional References for Repeated Dose Toxicity Studies:	None

5.3. Genetic Toxicity:

5.3.1. *In Vitro* Gene Mutations

Identity:	Fyrol 6; CAS# 2781-11-5; Lot # 49; purity not given
Method:	Ames test
Type:	Reverse mutation assay
GLP:	Yes
Year:	1978
Cell Type:	Salmonella typhimurium TA1535, TA1537, TA 1538, TA98, TA100; S. cerevisiae D4
Metabolic Activation:	Rat and mouse S9 induced by Aroclor 1254 or phenobarbital
Concentrations Tested:	With/Without S9:0.01-10 ul/plate
Vehicle:	Dimethyl sulfoxide
Cytotoxic Concentration:	No toxicity at any concentration.
Genotoxic Effects With Metabolic Activation:	None

Genotoxic Effects Without Metabolic Activation:	None
Conclusions:	Fyrol 6 was not mutagenic in Salmonella typhimurium strains TA1535, TA1537, TA1538, TA98, TA100 or S. cerevisiae strain D4 in the presence or absence of metabolic activation.
Reliability:	1
Reference:	15
Remarks:	None
Additional References for In Vitro Gene Mutation Studies:	None

Identity:	Fyrol 6; CAS# 2781-11-5; Lot # 49; purity not given
Method:	Mouse lymphoma assay
Type:	Forward mutation assay
GLP:	Yes
Year:	1978
Cell Type:	Mouse lymphoma cell line L5178Y
Metabolic Activation	Rat S9 induced by Aroclor 1254
Concentrations Tested:	With S9: 0.626-2.5 uL/mL Without S9: 1.25-5 ul/mL
Vehicle:	Sterile water
Cytotoxic Concentration:	Cytotoxic at 2.5 and 5 ul/mL
Genotoxic Effects With Metabolic Activation:	Weakly mutagenic
Genotoxic Effects Without Metabolic Activation:	Weakly mutagenic
Conclusions:	Fyrol 6 was weakly mutagenic in the presence and absence of metabolic activation.
Reliability:	1
Reference:	16
Remarks:	None
Additional References for *In Vitro* Mutagenicity Studies:	None

Identity:	Fyrol 6; CAS# 2781-11-5; Lot # 1106C-1-3; purity not given
Method:	Mouse lymphoma assay
Type:	Forward mutation assay
GLP:	Yes
Year:	1981
Cell Type:	Mouse lymphoma cell line L5178Y
Metabolic Activation	Rat S9 induced by Aroclor 1254
Concentrations Tested:	With S9: 0.25-1.0 uL/mL Without S9: 0.0313-0.5 ul/mL
Vehicle:	Sterile water
Cytotoxic Concentration:	Cytotoxic at 0.5 ul/mL
Genotoxic Effects With Metabolic Activation:	Weakly mutagenic
Genotoxic Effects Without Metabolic Activation:	Weakly mutagenic
Conclusions:	Fyrol 6 was weakly mutagenic in the presence and absence of metabolic activation.
Reliability:	1
Reference:	17
Remarks:	None
Additional References for *In Vitro* Mutagenicity Studies:	None

5.3.2. *In Vitro* Chromosome Aberrations

Identity:	Fyrol 6; CAS# 2781-11-5; Lot # 1106C-1-3; purity not given
Method:	Mouse lymphoma assay
Type:	Chromosome aberration
GLP:	Yes
Year:	1982
Cell Type:	Mouse lymphoma cell line L5178Y
Metabolic Activation	Rat S9 induced by Aroclor 1254
Concentrations	With S9: 0.25-2.0 uL/mL

Tested:	Without S9: 0.0313-0.5 ul/mL
Vehicle:	Sterile water
Cytotoxic Concentration:	None
Genotoxic Effects With Metabolic Activation:	Clastogenic. Both structural and numerical chromosome aberrations were seen in the two highest dose groups.
Genotoxic Effects Without Metabolic Activation:	Clastogenic. Both structural and numerical chromosomal aberrations were seen in the two highest dose groups.
Conclusions:	Fyrol 6 was clastogenic in the presence and absence of metabolic activation.
Reliability:	1
Reference:	18
Remarks:	A statistically significant increase in structural and numerical aberrations was reported.
Additional References for *In Vitro* Chromosome Abberration Studies:	None

In Vitro Transformation

Identity:	Fyrol 6; CAS# 2781-11-5; Lot # 49; purity not given
Method:	BALB/3T3 Cell assay
Type:	In vitro transformation assay
GLP:	Yes
Year:	1978
Cell Type:	BALB/3T3 cells
Metabolic Activation	Not applicable
Concentrations Tested:	0.02-0.312 uL/mL
Vehicle:	Medium
Cytotoxic Concentration:	None
Genotoxic Effects With Metabolic Activation:	None
Genotoxic Effects Without Metabolic Activation:	None
Conclusions:	Fyrol 6 was not active in this assay.

Reliability:	1
Reference:	19
Remarks:	The cells were examined after a 72 hour exposure period and 3-4 week growth period
Additional References for *In Vitro* Trans-formation Studies:	None

5.4 Neurotoxicity

Identity:	Fyrol 6; CAS# 2781-11-5; Lot# 0106E-2-2; purity – 97.4%
Method:	Fed. Reg. 43 (163):37362-37363, 1978
Type:	Acute Delayed Neurotoxicity
GLP:	Yes
Year:	1982
Species/Strain:	Hen/White Leghorn
Sex:	F
No. Of Animals Per Sex Per Dose:	10
Vehicle:	Corn oil
Route of Administration:	Oral gavage
Time of Observation Period:	43 Days
Doses Administered:	1 or 10 g/kg
Frequency of Treatment:	Two doses, three weeks apart
NOAEL (NOEL):	10 g/kg x 2
LOAEL (LOEL):	None
Toxic Response By Dose Level:	None
Conclusions:	Fyrol 6 administered to hens did not cause delayed neurotoxicity at doses up to 10 g/kg administered 3 weeks apart.
Reliability:	1
Reference:	20
Remarks:	Tri-ortho-cresyl phosphate was used as the positive control. Clinical and histopathology evaluation was done.
Additional References for Repeated Dose Toxicity Studies:	None

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